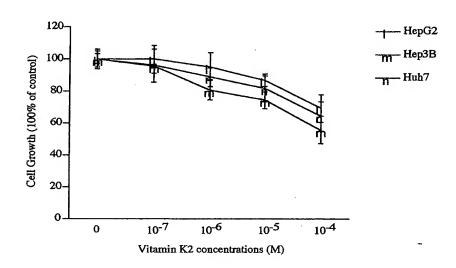
Sheet 1 of 9 Appl. No. To be assigned (U.S. National Phase of PCT/JP2004/006038, Int'l Filing Date: April 23, 2004); Dkt No. 1089.0580000/MAC/SJE; Inventors: OZAKI et al; For: MMP Expression Inhibitor

FIG. 1(a)

Effect of Vitamin K2 (48 h) on the proliferation of HCC cells



Effect of Vitamin K2 on the expression of the cyclin dependent kinase (Cdk) inhibitiors (p27, p21, p16)

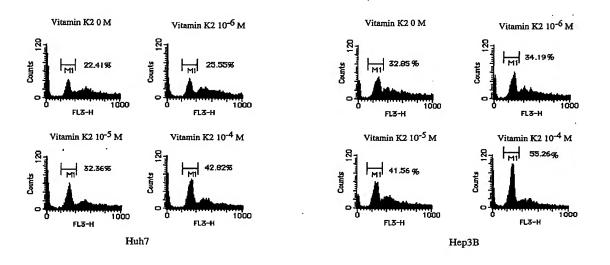
FIG. 1(b)

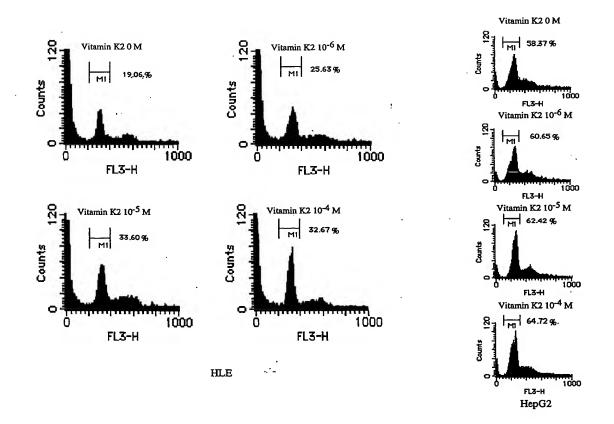
RT-PCR HepG2 Нер3В Huh7 0 10-6 10-5 10-4 (M) 0 10-6 10-5 10-4 (M) 0 10-6 10-5 10-4 (M) ←p27 -p27 ←p21 **←**p16 **←**p16 ←p16 ←GAPDH ←GAPDH ←GAPDH FIG. 1(c) Western blot 10-6 10-5 10-4 (M) 10-6 10-5 10-4 (M) -p27

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FIG.2

Vitamin K2 inhibited HCC cells proliferation through G1 arrest

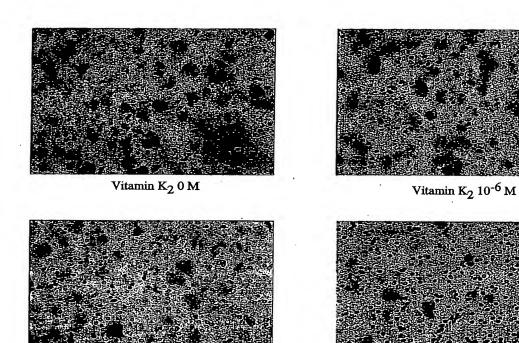




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FIG.3

Vitamin K2 dose-dependently inhibit the invasiveness of HepG2 cells

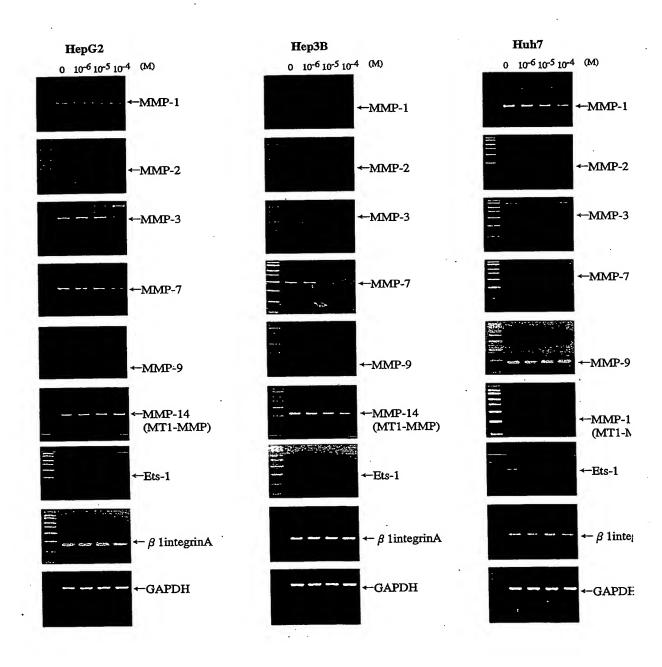


Vitamin K₂ 10⁻⁵ M

Vitamin $K_2 10^{-4} M$

FIG.4

Effect of Vitamin K2 on the mRNA expression of some invasion-related fact



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Vitamin K2 inhibit the expression of MMP-1 and MMP-3 protein in hepatoma cells

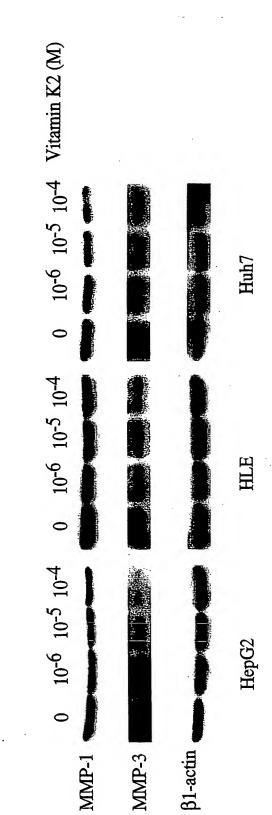
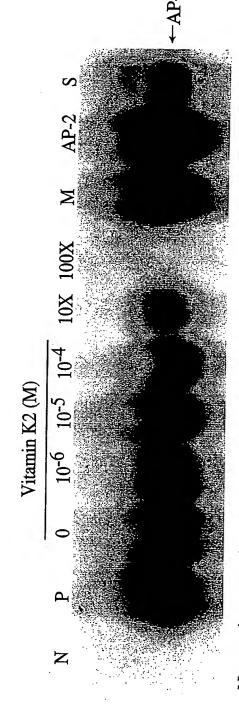


FIG.5

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Effect of Vitamin K2 on AP-1 transcriptional factor by Gel Shift



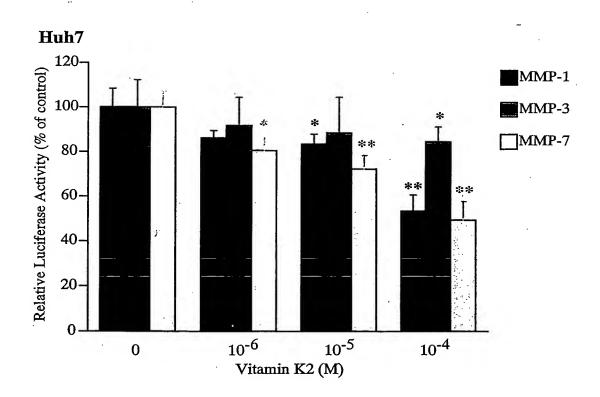
N: negative control, no nuclear extract
P: positive control, HeLa cells extract
10X: 10 times no labeled AP-1 competitor
100X: 100 times no labeled AP-1 competitor
M: mutant AP-1 oligo

S: super shift

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FIG.7

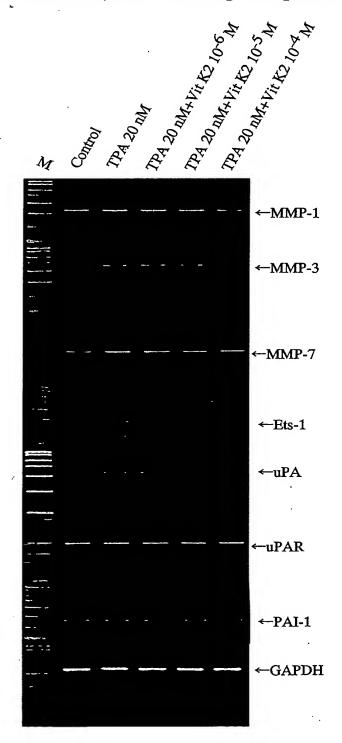
Vitamin K2 inhibit MMP promoter activity in HCC cells



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FIG.8

Vitamin K2 inhibits TPA induced invasion-related gene expression in HepG2 cells



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FIG.9

Vitamin K2 inhibits TPA-induced MMP expression in HepG2 cells

